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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,000	POLVERINO ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004 and 30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,13,14,16,46,47,57 and 59-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *13,16, and 57* is/are allowed.

6)☒ Claim(s) *9, 14, 46, 47, and 59-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 30, 2004 has been entered.

1. The amendment filed June 30, 2004 has been entered. Claims 15, 58, and 62 have been canceled. Claims 46, 59, and 60 have been amended.

2. The notice of appeal filed June 30, 2004 is acknowledged and has been entered.

3. Claims 9, 13, 14, 16, 46, 47, 57, and 59-61 are pending in the application.

Grounds of Objection Withdrawn

4. Unless specifically reiterated below, Applicant's amendment filed June 30, 2004 has obviated the grounds of objection set forth in the previous Office action mailed December 31, 2004.

Response to Amendment

5. After reconsideration, the indicated allowability of claims 9, 14, and 61 set forth in the previous Office action is withdrawn in view of following new grounds of rejection.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 9 and 59 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 9 and 59 are drawn to a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 5, which is produced by a recited process that optionally includes a step of isolating the polypeptide.

A polypeptide having the amino acid sequence of SEQ ID NO: 5 is disclosed as occurring naturally in human cells; see, e.g., page 85, line 19, through page 92, line 4; and the sequence listing.

Claims 9 and 59 are recognized as product-by-process claims, but the naturally occurring polypeptide of SEQ ID NO: 5 cannot be distinguished from the claimed polypeptide of SEQ ID NO: 5, since absent a showing of any difference, the claimed product and the naturally occurring product are the same polypeptide, which comprises the amino acid sequence of SEQ ID NO: 5. Moreover, as the claims presently read, because the polypeptide is not necessarily isolated, the process by which the claimed product is produced will not produce a protein that differs from the naturally occurring polypeptide of SEQ ID NO: 5.

Notably, in contrast to claim 59, claim 60 recites the host cell is a prokaryotic cell, which does not naturally produce the human polypeptide of SEQ ID NO: 5. Furthermore, the specification discloses that the human Secs-1 polypeptide of SEQ ID NO: 5 is N-glycosylated at position 51 (page 86, lines 12 and 13); therefore, a product produced according to the process recited in claim 60 would differ from the naturally occurring polypeptide of SEQ ID NO: 5, which is glycosylated. However, with regard to claims 9 and 59, which recite or encompass a polypeptide comprising SEQ ID NO: 5 produced by a process comprising culturing a eukaryotic cell, because a polypeptide comprising SEQ ID NO: 5 occurs naturally in cultured eukaryotic cells, absent a showing of any difference, the process recited in the claims will produce a product identical to or indistinguishable from the naturally occurring product. Because claims 9 and 59 encompass a naturally occurring product, the claims are directed to non-statutory subject matter.

This issue can be remedied by amending claim 9 to recite the term "isolated" before "polypeptide" in line 1 of the claim.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 14, 46, 47, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 is drawn to a polypeptide comprising a fragment of the amino acid sequence set forth as SEQ ID NO: 5, which fragment comprises at least about 25 amino acid residues, but not more than 80 amino acid resides, and, upon injection into an animal, produces an antibody that binds the polypeptide of SEQ ID NO: 5; and claims 46 and 47 are drawn to a fusion polypeptide comprising the polypeptide of claim 14 fused to a heterologous amino acid sequence.

Claim 61 is drawn to a polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence of a region of the nucleotide sequence of either (a) SEQ ID NO: 4 or (b) a DNA insert encoding a Secs-1 polypeptide, which insert is contained in the material deposited under ATCC Accession No. PTA-1755, wherein said nucleic acid molecule encodes a polypeptide fragment of at least about 25 amino acid residues, but not more than 80 amino acid resides, and, upon injection into an animal, produces an antibody that binds the polypeptide of SEQ ID NO: 5. Claim 61 is interpreted as "open", because the nucleic acid molecule encoding the claimed polypeptide *comprises* a nucleotide sequence encoding at least 25, but not more than 80 amino acids of SEQ ID NO: 5, such that the genus of claimed polypeptides is not limited to polypeptides that consist of fragments of the Secs-1 polypeptide of SEQ ID NO: 5 but includes polypeptides comprising at least 25, but not more than 80, amino acids of SEQ ID NO: 5.

The polynucleotide sequence of SEQ ID NO: 4 and the polynucleotide sequence of the DNA insert encode the Secs-1 polypeptide of SEQ ID NO: 5, so a nucleic acid molecule comprising a portion of SEQ ID NO: 4 or a portion of the DNA insert is capable of encoding a polypeptide comprising a mere fragment of SEQ ID NO: 5, which is at least about 25 amino

acids in length, but not more than 80. Although claims 14 and 61 recite a limitation requiring a polypeptide consisting of such a fragment of SEQ ID NO: 5 to elicit the production of an antibody that binds the intact Secs-1 polypeptide of SEQ ID NO: 5, because the claims encompass a genus of polypeptides that differ markedly in both structure and function, and share only a epitope recognized by an antibody against the polypeptide of SEQ ID NO: 5, but the presence of which does not correlate with the presence of any other particularly identifying structural or functional feature, the description of the polypeptide of SEQ ID NO: 5 is not deemed representative of at least a substantial number of those members.

Again, the claimed genus of polypeptides includes broadly varying members having an amino acid sequence that comprises a portion of the amino acid sequence of SEQ ID NO: 5, which is only about 25 to no more than 80 amino acids in length and is sufficiently immunogenic to produce an antibody that binds to the polypeptide of SEQ ID NO: 5 and the polypeptide comprising only a portion of that amino acid sequence.

Notably the members of the claimed genus of polypeptides, themselves, do not have to elicit the production of antibody that binds the polypeptide of SEQ ID NO: 5, but merely have to comprise a fragment of the amino acid sequence of SEQ ID NO: 5, which does so. Moreover, although each member of the claimed genus of polypeptides necessarily comprises the amino acid sequence of an epitope of SEQ ID NO: 5, because the amino acid sequence of the epitope may be "buried" in the three-dimensional structure of the polypeptides, and therefore not be "solvent-accessible", or immunogenic, the polypeptides, as they naturally fold, may not be capable of producing an antibody that binds to SEQ ID NO: 5.

Even if the claimed polypeptide, itself, produces an antibody that binds the polypeptide of SEQ ID NO: 5, because the presence of the common amino acid sequence of the epitope recognized by the cross-reactive antibody is not correlated to any particularly identifying substantial structural or functional feature, apart from a polypeptide comprising SEQ ID NO: 5 and a polypeptide comprising at least a portion of the polypeptide of SEQ ID NO: 5, which confers an ability to function as does the polypeptide of SEQ ID NO: 5, the skilled artisan could not immediately envision or recognize members of the claimed genus.

Although a polypeptide may have the amino acid of an epitope of the polypeptide of SEQ ID NO: 5, which is recognized by a cross-reactive antibody, the polypeptide may not have a

structure or a function that is even remotely similar to the polypeptide of SEQ ID NO: 5, since the members of the claimed genus of polypeptides have at most a common amino acid sequence that is 80 amino acids in length. Even if the members of the claimed genus of polypeptides were to have a more substantial identity with SEQ ID NO: 5, Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000), for example, discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Skolnick et al. teaches, even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept an assertion, which is based only upon an observed similarity in amino acid sequence or the presence of a common epitope recognized by a cross-reactive antibody, that a variant of the polypeptide of SEQ ID NO: 5 is capable of functioning the same, or even as having the same substantial structure as the polypeptide of SEQ ID NO: 5.

In deciding *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the Court held that a generic statement that defines a genus of nucleic acids *by only their functional activity* does not provide an adequate written description of the genus. By analogy, a generic statement that defines a genus of polypeptides by only the presence of a common amino acid sequence, which can elicit the production of antibody that cross-reactively binds the polypeptide of SEQ ID NO: 5, does not serve to adequately describe the genus as whole. The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Applicant has only described a single member of the claimed genus of polypeptides, namely the Secs-1 polypeptide of SEQ ID NO: 5. As presently claimed, SEQ ID NO: 5 is not representative of at least a substantial number of the members of the claimed genus of polypeptides, since the members of the genus are not described as sharing a particularly identifying and substantial structural feature, also common to the polypeptide of SEQ ID NO: 5, which correlates with a functional attribute of the polypeptide of SEQ ID NO: 5 and which is also shared by most other members. Accordingly, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the claimed polypeptides; and therefore the written description of the claimed invention would not suffice to reasonably convey Applicant's possession of the claimed invention at the time the application was filed.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 9 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Marchis-Mouren et al. (*Biochimie*. 1988 May; **70** (5): 663-671).

Claims 9 and 59 are drawn to a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 5, which is produced by a recited process that optionally includes a step of isolating the polypeptide.

Marchis-Mouren et al. teaches a human colon cancer cell line, namely HT-29, which, absent a showing otherwise, is deemed to produce upon culture a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 5; see entire document (e.g., the abstract).

Claims 9 and 59 are recognized as product-by-process claims, but the naturally occurring polypeptide of SEQ ID NO: 5, which is produced by cultured human cells, including, for example, those of the prior art, cannot be distinguished from the claimed polypeptide of SEQ ID NO: 5. The claimed product and the naturally occurring product are the same polypeptide, which comprises the amino acid sequence of SEQ ID NO: 5. Moreover, because the polypeptide produced according to the recited process is optionally, or not necessarily isolated, the process by which the claimed product is produced will not produce a protein that differs from the naturally occurring polypeptide of SEQ ID NO: 5.

Absent a showing of any difference, therefore, the cell line of the prior art upon culture, produces a polypeptide that comprises SEQ ID NO: 5 and is that same as, or indistinguishable from the polypeptide produced according to the processes recited in claims 9 and 59.

Conclusion

12. Claims 13, 16, and 57 are allowed. Claims 9, 14, 46, 47, and 59-61 have been rejected.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings,
Examiner
Art Unit 1642

slr
November 12, 2004